

WHAT IS CLAIMED IS:

- 1 1. A method, comprising:
 - 2 introducing an exogenous fluorescent contrast agent into a biologic tissue, the
 - 3 tissue multiply scattering light with a mean time-of-flight, and the agent having a
 - 4 fluorescence lifetime within a factor of about ten of the mean time-of-flight;
 - 5 exposing the tissue to an excitation light with a predetermined time-varying
 - 6 intensity;
 - 7 detecting a light emission from the tissue in response to said exposing;
 - 8 generating an image of the tissue by mapping spatial variation of a level of a fluorescence
 - 9 characteristic of the tissue from the light emission in accordance with a mathematical
 - 10 expression modeling multiple light scattering behavior of the tissue; and
 - 11 wherein the agent is selected in accordance with a predetermined relationship
 - 12 between degree of image contrast and at least one of fluorescence yield or the
 - 13 fluorescence lifetime.
- 1 2. The method of claim 1, wherein the at least one is fluorescence lifetime.
- 1 3. The method of claim 1, wherein the fluorescence lifetime is in a range of
- 2 about 0.1 to 10 nanoseconds.
- 1 4. The method of claim 1, wherein the fluorescence lifetime is in a range of
- 2 about 0.5 to 5 nanoseconds.
- 1 5. The method of claim 1, wherein the fluorescence lifetime is in a range of
- 2 about 0.2 to 2 nanoseconds.
- 1 6. The method of claim 1, wherein the mathematical expression corresponds
- 2 to a diffusion equation approximation of multiply scattered light.
- 1 7. The method of claim 1, wherein the fluorescence characteristic is at least
- 2 one of fluorescence lifetime, fluorescence yield, or fluorescence quantum efficiency.
- 1 8. The method of claim 1, wherein said generating includes determining a
- 2 modulation amplitude change and a phase change of the light emission relative to the
- 3 excitation light.
- 1 9. The method of claim 8, wherein the fluorescence characteristic
- 2 corresponds to the fluorescence lifetime.

1 10. The method of claim 9, wherein the mathematical expression is in a
2 frequency domain form and the image contrast is provided in terms of at least one of
3 phase shift contrast or modulation contrast.

1 11. A method comprising:
2 selecting a fluorescent contrast agent as a function of a predetermined time-of-
3 flight for a tissue to be imaged in accordance with a mathematical expression modeling
4 the behavior of multiply scattered light traveling through the tissue, the fluorescent
5 contrast agent have a fluorescence lifetime within a factor of ten of the predetermined
6 time-of-flight; and

7 providing the fluorescent agent for introduction into the tissue.

1 12. The method of claim 11, wherein the fluorescence lifetime is in a range of
2 about 0.1 to 10 nanoseconds.

1 13. The method of claim 11, wherein the fluorescence lifetime is in a range of
2 about 0.5 to 5 nanoseconds.

1 14. The method of claim 11, wherein the fluorescence lifetime is in a range of
2 about 0.2 to 2 nanoseconds.

1 15. The method of claim 11, wherein the mathematical expression
2 corresponds to a diffusion equation approximation of multiply scattered light.

1 16. The method of claim 11, further comprising generating an image of the
2 tissue by mapping spatial variation of a level of a fluorescence characteristic of the tissue.

1 17. A method, comprising:
2 evaluating ability of a number of fluorescent agents to provide image contrast
3 between different tissue types, said evaluating including determining a relationship
4 between degree of image contrast and at least one of fluorescence lifetime or
5 fluorescence yield of the agent;

6 selecting one of the agents based on said evaluating; and

7 providing the selected one of the agents for introduction into a biologic tissue to
8 enhance imaging performed in accordance with a mathematical expression modeling the
9 behavior of multiply scattered light traveling through the tissue.

1 18. The method of claim 17, wherein the at least one is fluorescence lifetime.

1 19. The method of claim 17, wherein the mathematical expression
2 corresponds to a diffusion equation approximation of multiply scattered light.

1 20. The method of claim 19, further comprising applying the diffusion
2 equation approximation in a frequency domain form.

1 21. The method of claim 17, further comprising generating an image of the
2 tissue by mapping spatial variation of a level of a fluorescence characteristic of the tissue.

1 22. The method of claim 17, wherein the mathematical expression is in a
2 frequency domain form and the image contrast is provided in terms of at least one of
3 phase shift contrast or modulation contrast.

1 23. A method, comprising:
2 exposing a biologic tissue to a first excitation light;
3 detecting a first emission from the tissue in response to the first excitation light;
4 introducing a fluorescent contrast agent into the tissue after said detecting;
5 exposing the tissue after said introducing to a second excitation light;
6 sensing a second emission in response to the second excitation light;
7 comparing data corresponding to the first emission with data corresponding to the
8 second emission to evaluate contrast provided by the agent as a function of at least one of
9 fluorescence lifetime, fluorescence yield, or quantum efficiency.

1 24. The method of claim 23, wherein the at least one is fluorescence lifetime.

1 25. The method of claim 24, wherein the fluorescence lifetime is in a range of
2 about 0.1 to 10 nanoseconds.

1 26. The method of claim 24, wherein the fluorescence lifetime is in a range of
2 about 0.5 to 5 nanoseconds.

1 27. The method of claim 24, wherein the fluorescence lifetime is in a range of
2 about 0.2 to 2 nanoseconds.

1 28. The method of claim 23, further comprising evaluating the first and
2 second emissions with a mathematical expression modeling the behavior of multiply
3 scattered light traveling through the tissue.

1 29. The method of claim 28, wherein the mathematical expression
2 corresponds to a diffusion equation approximation of multiply scattered light.

1 30. The method of claim 23, further comprising generating an image of the
2 tissue by mapping spatial variation of a level of a fluorescence characteristic of the tissue.

1 31. The method of claim 30, wherein the fluorescence characteristic is at least
2 one of fluorescence lifetime, fluorescence yield, or fluorescence quantum efficiency.

1 32. The method of claim 30, wherein said generating includes determining a
2 modulation amplitude change and a phase change of the light emission relative to the
3 excitation light.

1 33. The method of claim 32, wherein the fluorescence characteristic
2 corresponds to the fluorescence lifetime.

1 34. The method of claim 23, wherein wavelength of the first excitation light is
2 generally the same as wavelength of fluorescent light emitted by the agent in response to
3 the second excitation light.